EXHIBIT 1

DECLARATION OF DR. BERT O'MALLEY

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

1. I have been working in the field of gene therapy, in particular, the regulation of transcription by steroid hormone receptors, for the more than 20 years.. I am the Tom Thompson Professor and Chairman, Department of Cell Biology and Director of the Baylor Center for Reproductive Biology, Baylor College of Medicine, Houston, TX, In addition, I am member of the National Academy of Sciences. My Curriculum Vitae is attached as Exhibit A.

2. I am a co-inventor on the patent application entitled, "Mutated Steroid Hormone Receptors. Methods for Their Use and Molecular Switch For Gene Therapy," serial number 08/454,418.

3. Experiments were performed in my laboratory that demonstrate the *in vivo* therapeutic effect of a plasmid construct regulated by the ligand-inducible gene switch described in the above-mentioned patent application. Briefly, a stable cell line was developed in my laboratory that expressed the tyrosine hydroxylase (TH) gene under the control of the gene switch. The details of the construction of this cell line are described in Exhibit B entitled, "A Regulatory System for Use in Gene Transfer" (PNAS 91:8180-8184, 1994). Rats were unilaterally dopamine depleted in striatum by injection of 6-hydroxydopamine. The degree of degeneration was confirmed by the rotational

response to apomorphine. The gene switch regulated cell line was implanted into the brain and the rotational response monitored following administration of RU486. As described in attached Exhibit B, RU486 activates tyrosine hydroylase expression in the inducible cell line and the effect of TH expression (and subsequent dopamine production) was monitored by a decrease in the rotational frequency of the lesioned rats. Exhibit C is a graph of the rotation frequency of one of the rats in the study demonstrating a significant reduction in apomorphine-induced rotation beginning approximately 30 min after intraperitoneal administration of RU486.

4. These data demonstrate the therapeutic benefit of a gene switch controlled system in a widely accepted model of Parkinson's disease and indicate that such treatment may be effective in humans.

5. The methodology described in the 08/454,418 application can readily be used to identify any member of the steroid hormone family of receptors that would have a phenotype like that of the specific progesterone mutant used in the above described animal studies. Since all of the members of the steroid hormone family of receptors have conserved functional domains which are modular in nature, one skilled in this area would be able to select the ligand binding domain of the receptor of interest, mutate the sequence by any of a number of well established methods and screen for the desired phenotype by this method.

6. The following papers have appeared in the literature since the filing of the 08/454,418 application. 1) Mahfoudi et al., 1995, Specific mutations in the estrogen receptor change the properties of antiestrogens to full agonists, PNAS 92:4206-4210; Montano

et al., 1996, Human estrogen receptors ligand activity mutants: receptors that interpret antiestrogens as estrogens and estrogens as antiestrogens and discriminate among different antiestrogens, Molecular Endocrinology 10:230-242; and Lanz and Rusconi, 1994, A conserved carboxy-terminal subdomain is important for ligand interpretation and transactivation by nuclear receptors Endocrinology 135:2183-2195 (Attached as Exhibit's D, E and F, respectively). These investigators have identified other members of the steroid hormone family of receptors (estrogen and glucocorticoid receptors) that have a similar agonist-inducible phenotype. All of these receptors mutant could be identified using the methodology described in the 08/454,418 application and confirm the representative nature of the discovery of the mutant phenotype first identified by my laboratory. In addition, these references demonstrate that multiple steroid hormone receptors can be used in a manner consistent with that claimed in the patent application.

I declare that all statements made herein are of my own personal knowledge are true and that all statements made on information and belief are believed true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of title 18 of the United States Code, and that such willful false statement may jeopardize the validity of the application or any patents issued thereon.

Date: 9/17/97

Bert W. O'Malley, M.D.